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Establishing Robust Left-Right Asymmetry in the Vertebrate Embryo

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One of the most surprising things to emerge in the study of left-right asymmetry is that the mechanism by which symmetry is first broken (which was thought of as the most fundamental problem in the field) is actually not conserved across different classes of vertebrates. However, what is conserved is the downstream use of Nodal as a key left-sided inductive signal and of Lefty as a negative feedback inhibitor. This paper, from Hiroshi Hamada and coworkers, provided insight into why the Nodal-Lefty system is so special and evolutionarily maintained as the key determinant of left-right patterning, from snails to echinoderms to birds to mammals. The regulatory and biophysical properties of Nodal and Lefty provide a reaction-diffusion-like mechanism that can amplify a relatively small bias in differential gene expression between the left and right sides of the embryo. Thus, the Nodal-Lefty system enhances the expression activity on the side where it is slightly stronger to begin with while concomitantly repressing the activity on the side where it is initially weaker. This mechanism elucidated by Hamada and colleagues can transform weak asymmetry (derived from any of a number of mechanisms, such as the directional rotation of cilia in mammals) into robust asymmetry.
This PaperPick refers to "Generation of robust left-right asymmetry in the mouse embryo requires a self-enhancement and lateral-inhibition system," by Tetsuya Nakamura, Naoki Mine, Etsushi Nakaguchi, Atsushi Mochizuki, Masamichi Yamamoto, Kenta Yashiro, Chikara Meno, and Hiroshi Hamada, published in October 2006.